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6: Wilson GB, Vertatschitsch EJ, Sarna SK, Sims SM. Related Articles

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7: Wilson GB, Fudenberg HH, Keller RH. Related Articles

Guidelines for immunotherapy of antigen-specific defects with transfer factor.
J Clin Lab Immunol. 1984 Feb;13(2):51-8.
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Effects of dialyzable leukocyte extracts with transfer factor activity on leukocyte migration in vitro. V. Antigen-specific lymphocyte responsiveness can be initiated by two structurally distinct polyribonucleopeptides.
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De novo initiation of specific cell-mediated immune responsiveness in chickens by transfer factor (specific immunity inducer) obtained from bovine colostrum and milk.

Wilson GB, Poindexter C, Fort JD, Ludden KD.

Amtron, Inc., Charleston, South Carolina.

Transfer factors (TF) were prepared from colostrum and milk of bovines previously immunized with antigens obtained from Coccidioides immitis, infectious bovine rhinotracheitis virus, or from the viral agents responsible for avian Newcastle disease, laryngotracheitis disease or infectious bursal disease. The ability of bovine TF to transfer specific cell-mediated immune responsiveness to a markedly xenogenic species was studied using specific pathogen free (SPF) and standard commercial (SC) chickens as model recipients. Cell-mediated immune responsiveness was documented using one or more of the following for each antigen (organism) studied: (a) an in vitro chicken leukocyte (heterophil) migration inhibition assay; (b) delayed-wattle reactivity; or (c) protection from clinical disease. Chicken TFs obtained from spleens of immune donors were evaluated in parallel to bovine TF's in selected comparative studies. Bovine TF also referred to as specific immunity inducer (SII), and chicken TF were found to initiate antigen-specific cell-mediated immunity de novo in previously non-immune SPF chickens as well as in SC chickens despite the presence of maternally acquired humoral antibody which may serve as a "barrier" to immunization of SC chickens when commercially available vaccines are administered by parenteral routes. Bovine TF's specific for laryngotracheitis virus or infectious bursal disease virus afforded protection equal to that found for commercially available vaccines. Bovine TF's action was rapid (less than a day) and of relatively long duration at least 35 days.

PMID: 2897772 [PubMed - indexed for MEDLINE]

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In vitro transfer of cellular immunity against nasopharyngeal carcinoma using transfer factor from donors with Epstein-Barr virus antibody activity.

Brandes LJ, Goldenberg GJ.

PMID: 4371172 [PubMed - indexed for MEDLINE]

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Epidermodysplasia verruciformis: response to therapy with dialyzable leukocyte extract (transfer factor) derived from household contacts.

Vasily DB, Miller OF, Fudenberg HH, Goust JM, Wilson GB.

Dialyzable leukocyte extracts (DLE) have been used to treat a variety of antigen selective, and broad spectrum immunodeficiency diseases with sometimes encouraging results. We describe here the clinical and laboratory responses to DLE therapy of 2 patients with epidermodysplasia verruciformis (EV), a chronic cutaneous infection with a variety of human papilloma viruses. One patient with longstanding (30 yr) disease and no improvement to previous therapy showed gradual yet definite resolution of extensive verrucae planae, plaque, tinea-versicolor-like, and tumor lesions scattered over his entire integument. Cessation of DLE therapy for a short time resulted in recurrence of partially regressed lesions and also in the development of new tumors in this patient. The second patient, a grandson of the first patient, with minimal disease showed no progression of the disease during DLE prophylaxis. A third subject (brother of patient number 2) received no DLE and served as a control. All 3 subjects demonstrated severely depressed levels of suppressor T cells, a defect in cell-mediated immunity that has not been hitherto reported in patients with EV. Finally, evidence is presented for a possible X-linked recessive mode of inheritance for susceptibility to EV.

PMID: 6086930 [PubMed - indexed for MEDLINE]

1: J Clin Lab Immunol 1984 Feb;13(2):51-8 Related Articles, Books

Guidelines for immunotherapy of antigen-specific defects with transfer factor.

Wilson GB, Fudenberg HH, Keller RH.

Dialyzable leukocyte extracts (DLE) containing transfer factor (TF) with documented specificity for one or more microbial antigens have shown previously variable clinical effectiveness in treating many infectious diseases caused by viruses, fungi, protozoa and mycobacteria. The efficacy has sometimes been strong, and at other times dubious, in treating patients with inherited or presumably "acquired" immunodeficiency diseases refractory to standard therapy. The recent development of assays for screening leukocyte donors of DLE, for monitoring recipients, and especially for determining the potency of various DLE preparations containing antigen-specific TF and for predicting the clinical course of disease have, in our hands, greatly improved the likelihood of successful immunotherapy with TF. Two representative cases are reported, one involving a patient with an antigen selective defect to Candida, and another involving a patient with an antigen selective defect to Mycobacterium fortuitum. Both patients responded as judged by laboratory tests and clinical improvement when treated with certain DLE preparations but not with others. Finally, certain DLE preparations appeared to suppress cell-mediated immunity in vivo and this suppression could be predicted by in vitro tests. Based on these results, guidelines for optimal therapy with DLE are proffered .

PMID: 6202873 [PubMed - indexed for MEDLINE]

1: Thymus 1984;6(3):167-80 Related Articles, Books

Dialyzable leukocyte extracts contain thymosin.

Wilson GB, Paddock GV, Floyd E, Newell RT, Dopson MH.

Trypsinization of human T-lymphocytes removes surface receptors which bind to sheep erythrocytes (E). Human dialyzable leukocytes extracts (DLE) and thymosin (Fraction V) have been shown to significantly increase the rate of regeneration of T-lymphocyte E-receptors. Both physical-chemical and immunochemical results reported herein indicate that the enhancing effect of human DLE preparations on the rate of regeneration of T-lymphocyte E-receptors is due at least in part to the presence of thymosin alpha 1-peptide in these preparations. Thymosin alpha 1-peptide purified from thymosin Fraction V and putative thymosin alpha 1 preparations purified from human DLEs were each active not only in increasing the rate of regeneration of T-lymphocyte E-receptors removed by trypsinization but also were active in vitro in markedly increasing the number of E-rosetting cells in two patients with immunodeficiency disease manifested in part as a reduction in the normal percentage of mature T-lymphocytes capable of forming E-rosettes.

PMID: 6464097 [PubMed - indexed for MEDLINE]

Treatment of Mycobacterium fortuitum pulmonary infection with "transfer factor" (TF): new methodology for evaluating TF potency and predicting clinical response.

Wilson GB, Metcalf JF, Fudenberg HH.

PMID: 7049471 [PubMed - indexed for MEDLINE]

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Bovine 'transfer factor': an oligoribonucleopeptide which initiates antigen-specific lymphocytes responsiveness.

Wilson GB, Paddock GV, Fudenberg HH.

Bovine transfer factor (TF)--active in initiating specific responsiveness in human thymus-derived (T) lymphocytes to purified protein derivative from Mycobacterium tuberculosis (PPD) in vitro--was partially purified from the dialyzable portion of medium from immune lymph node cells (DLNE). Its physiochemical properties and structure were determined by methods previously employed to characterize human PPD-specific TF isolated from dialyzable leukocyte extracts (DLE). Bovine TF had a molecular weight (MW) of 1100-3000, was destroyed by heating at 56 or 80 degrees C for 30 min, was soluble in water but not in phenol or ether, and could be precipitated with ethanol. Bovine TF activity eluted as a single peak after high-pressure reverse-phase liquid chromatography (HPLC); the active moiety contained at least one free co-planar cis-diol group, as shown by boronate affinity chromatography. Additional structural features were deduced by evaluating TF activity after incubation with various endonucleases, exonucleases, and peptidases, a phosphatase, and a protease. The combined results indicate that bovine TF specific for PPD is an oligoribonucleopeptide. A simplest case molecular model was constructed on the basis of the data obtained. A comparative evaluation of the physicochemical properties and structural features of bovine TF and human TF specific for PPD indicated striking similarities and some differences.

PMID: 6191411 [PubMed - indexed for MEDLINE]

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Effects of dialyzable leukocyte extracts with transfer factor activity on leukocyte migration in vitro. V. Antigen-specific lymphocyte responsiveness can be initiated by two structurally distinct polyribonucleopeptides.

Wilson GB, Paddock GV, Fudenberg HH.

Human transfer factors (TF) active in specifically inducing responsiveness in human thymus-derived (T) lymphocytes previously nonresponsive to purified protein derivative from Myobacterium tuberculosis (PPD) or to Coccidioides immites (Cocci) in vitro were isolated from the dialyzable portion of extracts of immune leukocytes (DLE). Each TF segregated into two active fractions after high-pressure reverse-phase liquid chromatography (HPLC), suggesting the presence of two TF components in DLE for each antigen specificity. Determination of the structures of both TF components specific for PPD was accomplished by evaluating their activity after incubation with various endonucleases, exonucleases, phosphatases, peptidases and a protease. The results indicated that both PPD-specific TF components are oligoribonucleopeptides but that they are structurally distinct. Simplest-case molecular models were constructed on the basis of the data obtained.

PMID: 6165106 [PubMed - indexed for MEDLINE]

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Chorioretinitis with a combined defect in T and B lymphocytes and granulocytes. A new syndrome successfully treated with dialyzable leukocyte extracts (transfer factor).

Kyong CU, Wilson GB, Fudenberg HH, Goust JM, Richardson P, Echerd J.

A patient with immune deficiency, recurrent pyogenic infections and active chorioretinitis is described; in addition to agammaglobulinemia, both quantitative and qualitative T-cell deficiencies were documented. Furthermore, the patient's granulocytes (polymorphonuclear leukocytes), although normal in their bactericidal capacity for Staphylococcus, responded poorly to both leukocyte migration inhibition factor and neutrophil immobilizing factor obtained from normal cells. The immunologic features of this patient appear to comprise a new syndrome. Remarkable diminution of the ocular lesions and increased visual acuity occurred within two months after the initiation of therapy with dialyzable leukocyte extracts (transfer factor). Concurrent testing of the patient's cell-mediated immunity showed increased numbers of circulating T lymphocytes and improved T-cell function following dialyzable leukocyte extract [DLE] therapy. The dramatic clinical results indicate that similar therapy may prove to be beneficial in other patients with chorioretinitis and T-cell deficiency.

PMID: 6992573 [PubMed - indexed for MEDLINE]

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Effects of dialyzable leukocyte extracts with transfer factor activity on leukocyte migration in vitro. II. Separation and partial characterization of the components in DLE producing antigen-dependent and antigen-independent effects.

Wilson GB, Fudenberg HH.

Previous studies have shown that DLEs with TFd activity produce both Ag-dependent specific effects (mediated by TFd) and Ag-independent effects on CMl as demonstrated in vitro by agarose LMl. In the present study, Sephadex G-25 gel filtration provided a simple method for separating the DLE components responsible for each effect into distinct fractions. Ag-independent LMl was produced predominantly by Sephadex fraction l, of MW greater than 5000. The active components, further purified on Bio-Gel P-10, were shown to be of MW 14,000 to 17,000 and to contain both polypeptide and ribonucliotide material. The Ag-independent LMl activity was stable to heating at 56 degrees C for 30 min but was partially destroyed at 80 degrees C for 30 min, and the responsible components were shown to act on PMN directly. Ag-independent ELM was produced exclusively by material in Sephadex G-25 fraction V and also acted directly on PMN, whereas the Ag-dependent specific LMl activity was found predominantly in fraction lVb and to a lesser extent in fraction V and could not be detected in a direct assay using only PMN. In addition, a new activity, designated "Ag-dependent ELM activity," which caused increased migration in the presence of Ag, was found in Sephadex fraction lVa. This latter activity might mask the Ag-dependent LMl activity in fraciton lVb. Bio-Gel P-2 chromatography separated the components producing Ag-dependent and Ag-independent effects in fraction V into two separate subfractions (Va and Vb) of MW 1100 to 2000 and less than 900. The activity in fraction lVb eluted at a position identical to that of the components in fraction Va on Bio-Gel P-2. Fractions Va and Vb contained both polypeptide and ribonucleotide material. The Ag-dependent specific LMl or TFd activity was found to be partially inactivated at 56 degrees C and completely destroyed at 80 degrees C. The components responsible for this TFd activity were further purified by HPLC on ODS resin. The TFd activity was mediated by components with retention times much greater than that of adenosine 3'-monophosphate. The active fraction was composed of both polypeptide and ribonucleotide material but did not contain deoxyribonucleotides.

PMID: 429877 [PubMed - indexed for MEDLINE]

Effects of dialyzable leukocyte extracts with transfer factor activity on leukocyte migration in vitro. 1. Antigen-dependent inhibition and antigen-independent inhibition and enhancement of migration.

Wilson GB, Fudenberg HH, Horsmanheimo M.

The effects of DLE containing TFd activity from immune human donors on PBL, obtained from individuals nonresponsive to either PPD or Cocci antigen, were evaluated in vitro by the agarose LMl technique. Several different preparations of DLE were employed to evaluate the specificity and reproducibility of the effects: (1) from donors skin test positive to PPD but negative to Cocci, (2) from donors skin test negative to PPD but positive to Cocci, (3) from donors skin test positive to both antigens, and (4) from donors skin test negative to both antigens. With PBL from other human donors used as target cells in the direct agarose LMi technique, three types of effects were demonstrated for all preparations of DLE: (1) antigen-dependent specific LMl, (2) antigen-independent or nonspecific LMl, and (3) antigen-independent enhancement of migration. The demonstration of each activity was found to depend on the concentration of DLE used and the time allowed for migration. In experiments employing purified PMN and MNL as target cells and a two-step indirect LMl assay, it was shown that the antigen-independent effects resulted from the direct of components in DLE on PMN. The antigen-independent inhibition was shown not to result from toxic effects of DLE. It was produced by DLE but not by dialyzable liver or skin extracts when tested using an amount equivalent to DLE as judged by the absorbance at 260 and 280 nm. The antigen-dependent LMl was found to require secretion of a soluble mediator of molecular weight near 69,000, believed to be LMl. Our results indicate that the agarose LMl technique is a useful in vitro assay for studies of the mechanism of action of components in DLE which can specifically convert nonimmune lymphocytes to a measurable antigen-sensitive state (i.e., transfer factor). The antigen-independent effects of DLE may be responsible in part for previously reported nonspecific beneficial effects of DLE when used in immunotherapy.

PMID: 429876 [PubMed - indexed for MEDLINE]

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IgE levels are the same in chronic fatigue syndrome (CFS) and control subjects when stratified by allergy skin test results and rhinitis types.
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Chronic fatigue syndrome (CFS) associated with Staphylococcus spp. bacteremia, responsive to potassium arsenite 0.5% in a veterinary surgeon and his coworking wife, handling with CFS animal cases.
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Cognitive and mood disturbance as causes and symptoms of fatigue in cancer patients.

Valentine AD, Meyers CA.

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Fatigue, cognitive dysfunction, and depression are very common in cancer patients. A relationship among the three entities is recognized but poorly understood. Factors that contribute to this poor understanding are the subjective nature of the symptoms, multiple potential causes, and a lack of reliable assessment tools. An understanding of fatigue in cancer patients may benefit from studies of chronic fatigue syndrome (CFS) and other nonmalignant diseases indicating that cognitive impairment varies with physical and mental fatigue, and that symptoms of depression experienced by patients with physical illnesses and primary mood disorders are qualitatively different. The multidimensional nature of fatigue suggests that interventions should be patient-specific. They could be related to lifestyle or involve the use of specific behavioral or pharmacologic therapies. As is the case with depression and cognitive disorders, targeted interventions against cancer-related fatigue will benefit from a better understanding of its potential biologic causes. Consideration of cognitive dysfunction and depression complicates the understanding of cancer-related fatigue; however, it provides opportunities to assist patients who must deal with this serious problem.

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